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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/690,639	10/23/2003	Juan Lopez de Silanes	2099.0010001/JAG/LAV	9165

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EXAMINER	
KIM, YUNSOO	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 12/15/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/690,639	DE SILANES ET AL.	
	Examiner	Art Unit	
	Yunsoo Kim	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 September 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *30,31,36,44-54,61-63,67 and 74-76* is/are pending in the application.

4a) Of the above claim(s) *46-54 and 61-63* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *30,31,36,44,45,67,74-76* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 30, 31, 36, 44-54, 61-63, 67 and 74-76 are pending.

Claims 46-54 and 61-63 stand withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b) as being drawn to nonelected invention/species.

Currently, claims 30, 31, 36, 44, 45, 67 and 74-76 are under consideration.

2. In view of applicants' amendment to the claims and remarks, the following rejections remain.

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 30, 31, 36, 44, 45, 67 and 74-76 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a composition comprising of a polyclonal antibody $F(ab')_2$ binds to a purified molecule or a mixture of antigenic molecules found in the venom of a scorpion; does not reasonably provide enablement for a **pharmaceutical** composition comprising of a polyclonal antibody $F(ab')_2$ binds to a purified molecule or a mixture of antigenic molecules from a venom of a scorpion and neutralizing venom. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and /or use the invention commensurate in scope with these claims.

Applicants' arguments filed 9/21/06 have been fully considered but they were not found persuasive. Applicants traversed the rejection based on that the breadth of the claims is enabled and adequate guidance in the specification is given as well as the working examples.

As discussed in the office action mailed 3/21/06, while being enabling a composition comprising an antibody binds to a purified molecule or a mixture of antigenic molecules found in the venom of a scorpion, the specification does not provide enablement for a pharmaceutical composition comprising a polyclonal antibody $F(ab')_2$ binds to venom of a scorpion and neutralizing venom.

It is at issue whether or not the claimed invention would function as pharmaceutical composition. In view of absence of a specific and detailed in Applicants' specification of how to effectively use the pharmaceutical composition comprising the polyclonal antibody $F(ab')_2$ as claimed, and absence of working examples providing evidence which is reasonably predictive that the claimed pharmaceutical composition are effective for in vivo use, and the lack of predictability in the art at the time the inventions was made, an undue amount of experimentation would be required to practice the claimed pharmaceutical composition with a reasonable expectation of success. Example 7, p. 23 of the instant application discloses in vivo experiment of venom of non-scorpion species. Moreover, the pharmaceutical composition is considered more than a mere purity or grade of a composition but should be suitable for in vivo use.

In addition, as discussed previously and taught by the references by Burton et al. (of record) and Vanlandschool et al. (of record), not all antibodies are neutralizing. The examples 3-8 of the specification are not directed to the scorpion antibodies. As described in the '976 patent (of record, col. 3, lines 18-50, in particular), not all animal venoms are equally feasible in prophylactic measures.

Applicants provide the definition of "neutralize" to mean "to render neutralize" and thus specification provides sufficient guidance to enable the practices of the claimed invention. However, there is no working examples of neutralizing activity of the composition comprising the antibody binds to the venom of a scorpion achieving the pertinent therapeutic effect given in the specification disclosure on p. 2.

Given the number of possibilities associated with neutralizing an antigenic molecule, including via direct or indirect effects associated with antigenic structure or function, as to whether such a desired effect can be achieved or predicted, as encompassed by the claim, it would take undue experimentation to practice the claimed invention.

To summarize, reasonable correlation must exist between the scope of the claims and scope of the enablement set forth. In view or the quantity of experimentation necessary, the limited working example, the unpredictability of the art, the lack of sufficient guidance in the specification, and the breath of the claims, it would take undue trials and errors to practice the claimed invention.

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

6. Claims 30, 31, 36, 44, 45, 67 and 74-76 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S.Pat. No. 5,443,976, of record, in view of U.S. Pat. No. 4,849,352 (IDS reference, of record) as evidenced by Harlow and Lane (Antibodies, 1988, Cold Spring Harbor Lab., p.298-299, of record) and Campbell (Monoclonal and Immunosensor Technology, 1991, Elsevier, vol. 23, p. 288-291, of record) for the reasons set forth in the office action mailed 3/21/06.

Applicants' arguments filed 9/21/06 have been fully considered but they were not found persuasive.

Applicants traversed the rejection based on that the '976 patent teach away from the claimed invention because the pepsin digestion and ammonium sulfate reduce yield of antibody and the potency is compromised (col. 6, lines 20-32).

However, the Applicants' argument that the '976 patent further teaches the general problem associated with using pepsin and ammonium sulfate reduces yield and potency is irrelevant. The problem that Applicants pointed out is associated with whole antibody. Use of polyvalent antibodies (col. 9, lines 11-40, in particular) solves the problem. In addition, the claimed invention is drawn to a pharmaceutical composition comprising antibody fragments that binds to a venom mixture of a scorpion.
Thus, even if the use of ammonium sulfate and pepsin reduces potency and yield, given that the claimed invention is a product claim, the patentability of a product does not depend on its method of production. MPEP 2113.

The '976 patent teaches IgY polyclonal antibody to a scorpion venom, *Centruroids noxius* (col. 11, lines 43, Example 52, in particular).

The '976 patent does not teach $F(ab')_2$ fragments.

However, the '352 patent teaches a pharmaceutical composition comprising a polyclonal $F(ab')_2$ binds to any antigen, pepsin digested followed by ammonium sulfate precipitation (col 3, lines 22-41, col. 2, lines 51-65, in particular).

The '352 patent further teaches that the antibody fragments are quickly distributed in the body, filtered and excreted by the kidney. Toxin neutralization by antibody fragments and volume circulating are greater than IgG (col. 1-2 overlapping paragraph, in particular).

The limitation " pharmaceutical" is met as the purified antibody after dialyzed against distilled water (e.g. pharmaceutically acceptable carrier, col. 8, lines 8-50, in particular) and 100ul of antibody injected to Swiss Webster mice (col. 11, lines 1-10, in particular). In addition, " substantially free of albumin, pyrogens and viral particles" is inherent property of any antibody purified by pepsin digestion and ammonium sulfate precipitation.

It is well known in the art as evidenced in Harlow and Lane (p. 299, in particular), repeating the precipitation process as necessary is within the optimization of procedures. Furthermore, the range of the first ammonium sulfate precipitation at about 16-22% and the second precipitation at about 32-38% is taught in Harlow and Lane as further evidenced by Campbell.

Campbell defines 100% saturated ammonium sulfate having 770g/l. Harlow and Lane suggest addition of 0.5 volume and to 50% saturation of saturated ammonium sulfate (step. 3, p. 29, in particualr) to antibody solution which results 1.5 total volume. The final concentration of ammonium sulfate is ~250g/l, which is equivalent to 25% by weight.

The concentration range of the second ammonium sulfate precipitation is met by addition of ammonium sulfate to 50% saturation (step 4), having 770g/l, 50% saturation is equivalent to 385g/l, or 38.5% by weight.

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to pepsin digest and purify with ammonium sulfate as taught by the '352 patent with the polyclonal and polyvalent antibody taught by the '976 patent.

The one of ordinary skill in the art would have been motivated to do so because the digestion with pepsin and purification with ammonium sulfate as taught by the '352 patent with the polyclonal and polyvalent combine antibody to scorpion venom *Centruroids noxius* taught by the '976 patent produces more readily utilizable antibody to scorpion venom. The '352 patent teaches intact IgG is too large to excreted by kidney functions and antibody fragments excrete many kinds of neurotoxins that are not accessible to IgG (col. 2, lines 22-50, in particular).

From the combined teachings of references, one of ordinary skill in art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of the ordinary skill in the art at the time the invention was made, as evidenced by references, especially in the absence of evidence to the contrary.

7. No claims are allowable.

8. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yunsoo Kim whose telephone number is 571-272-3176. The examiner can normally be reached on Monday thru Friday 8:30 - 5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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